

- 16 -

**We Claim:**

1. Use of a glutathione-increasing compound and a nitric oxide increasing compound in the manufacture of a medicament useful in the treatment of insulin resistance.
2. Use of a glutathione-increasing compound and a nitric oxide-increasing compound in improving glucose uptake in a patient suffering from insulin resistance.
3. Use of claim 1 or 2 wherein the insulin resistance is hepatic insulin sensitizing substance ("HISS")-dependent insulin resistance.
4. Use of claim 1, 2 or 3 wherein the glutathione-increasing compound is at least one of N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxylate ("OTC"), gamma glutamylcysteine and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cystine, cysteine, methionine, and S-adenosylmethionine ("SAdMe").
5. Use of claim 1, 2, 3 or 4 wherein the nitric oxide-increasing compound is at least one of SIN-1, molsidamine, nitrosylated N-acetylcysteine, nitrosylated cysteine esters, nitrosylated L-2-oxothiazolidine-4-carboxylate (NOTC), nitrosylated gamma glutamylcystine and its ethyl ester, nitrosylated glutathione ethyl ester, nitrosylated glutathione isopropyl ester, nitrosylated lipoic acid, nitrosylated cysteine, nitrosylated cystine, nitrosylated methionine, or nitrosylated S-adenosylmethionine.
6. A pharmaceutical composition comprising a hepatic glutathione increasing compound and a hepatic nitric oxide-increasing compound.
7. A pharmaceutical composition comprising at least one of nitrosylated N-acetylcysteine, nitrosylated cysteine esters, nitrosylated L-2-oxothiazolidine-4-carboxylate (NOTC), nitrosylated gamma glutamylcystine and

- 17 -

its ethyl ester, nitrosylated glutathione ethyl ester, nitrosylated glutathione isopropyl ester, nitrosylated lipoic acid, nitrosylated cysteine, nitrosylated cystine, nitrosylated methionine, or nitrosylated S-adenosylmethionine.

8. The pharmaceutical composition of claim 6 or 7 further including a pharmaceutically acceptable antioxidant.

9. A method of reducing insulin resistance in a mammalian patient having lower than normal hepatic glutathione levels, said method comprising:

selecting a patient suffering from insulin resistance;

determining if hepatic glutathione levels are lower than normal in the patient; and

administering a compound which increases hepatic glutathione and a compound which increases hepatic nitric oxide.

10. A method of reducing insulin resistance in a mammalian patient comprising administering a compound which increases hepatic glutathione and a compound which increases hepatic nitric oxide ("NO").

11. The composition of claim 6, 7 or 8 further including a pharmaceutically acceptable liver-targeting substance.

12. The method of claim 9 wherein the insulin resistance is HISS-dependent insulin resistance ("HDIR").

13. The method of claim 12 wherein the hepatic glutathione-increasing compound administered causes an increase in hepatic glutathione synthesis.

14. The method of claim 10, 11 or 12 wherein the glutathione-increasing compound is at least one of N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxylate ("OTC"), gamma glutamylcysteine and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cystine, cysteine, methionine, and S-adenosylmethionine ("SAME").

- 18 -

15. The method of claim 10, 11, 12, 13 or 14 wherein the nitric oxide-increasing compound is at least one of SIN-1, molsidamine, nitrosylated N-acetylcysteine, nitrosylated cysteine esters, nitrosylated L-2-oxothiazolidine-4-carboxylate (NOTC), nitrosylated gamma glutamylcystein and its ethyl ester, nitrosylated glutathione ethyl ester, nitrosylated glutathione isopropyl ester, nitrosylated lipoic acid, nitrosylated cysteine, nitrosylated cystine, nitrosylated methionine, or nitrosylated S-adenosylmethionine.
16. The method of any preceding claim wherein the glutathione-increasing compound is administered orally.
17. The method of any preceding claim wherein the glutathione-increasing compound is administered by intravenous injection.
18. The method of any preceding claim wherein the glutathione-increasing compound is 8-bromo-cGMP.
19. The method of any preceding claim wherein the compound which increases hepatic NO is administered orally.
20. The method of any preceding claim wherein the compound which increases hepatic NO is administered by intravenous injection.
21. The method of any preceding claim wherein the compound which increases nitric oxide is SIN-1.
22. The method of any preceding claim wherein the compound which increases hepatic NO is molsidamine.
23. The method of any preceding claim further including administering a pharmaceutically acceptable anti-oxidant.

- 19 -

24. The method of any preceding claim wherein the patient suffers from at least one of non-insulin dependent diabetes, essential hypertension, metabolic obesity, chronic liver disease, fetal alcohol effects, old age and a chronic inflammatory disease.

25. The method of any preceding claim wherein the patient is a human.